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Kidney stone clinic: ten years of experience

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The metabolic background of kidney stones has been recognized for many years.
The role of the clinical chemist in this particular disorder is essential, due to his responsibility for the organisation of metabolic investigations, risk assessment, and - in certain circumstances - monitoring in direct care, including treatment (1). Experiences are described at the kidney stone clinic in the Kladno Hospital, which operates in close cooperation with the Department of Urology.

Key-words: kidney stones, hypercalciuria, hyperuricosurie, thiazides, allopurinol

Investigation protocols

The kidney stone clinic was established in the mid-eighties as an integral part of the Department of Clinical Biochemistry. Initially, (1983-1985) the investigation protocol was based on the patient's stay in the hospital for several days. This protocol included:
- two 24-hour collections of urine during calcium and sodium restriction;
- two fasting venous blood samples;
- oral calcium tolerance test according to Pak's schedule.

This relatively complicated protocol was replaced by a new one which was more focused on an ambulatory system of investigation. At present, the protocol for out-patients is as follows:
1. Patients, including those with a first episode of stone appearance, are sent to the kidney stone clinic by the urologist, with written information on what is going to be done and how the urine has to be collected.
2. Patients are instructed to collect urine over a 24-hour period (Sunday).
3. Patients visit the kidney stone clinic on Monday morning, are asked questions about the history of their illness, and appropriate venous blood samples are taken by laboratory staff members.
4. Patients are informed of the date and time of subsequent consultation (usually the following Monday or Tuesday, 30 minutes per patient).

Parameters currently measured are:
Urine (24 hours) - sodium, potassium, calcium, magnesium, phosphate, creatinine, urate, oxalate, pH.
Morning urine - pH, citrate, creatinine, in certain cases hydroxyproline.
Serum - sodium, potassium, chloride, calcium, magnesium, phosphate, urea, creatinine, urate, alkaline phosphatase, proteins, albumin, glucose, cholesterol, triglycerides.
In certain clinical conditions, PTH, isoenzymes of alkaline phosphatase, osteocalcin, collagen derivates, liver enzymes or other parameters are measured too.
The results are processed by means of our own computing program, which provides all the necessary calculations. The report is embellished by the physician with written comments, conclusions and recommendations. During consultation with the patient, appropriate fluid intake and the dietary regimen is explained and recommended to the patient, together with the prescription of necessary drugs. Finally, the next visit of the patient is planned (usually 6 months or one year later). Then the patient visits his urologist with the report.

Table 1. Comparison of tested groups

	Group I	Group II	Group III
dU-Ca	7.71 (486)	4.83 (265)	4.51 (137)
mmol/d	7.28 ± 3.25	4.53 ± 2.65	4.50 ± 2.78
S-urate	308.0 (476)	254 (243)	268.6 (132)
µmol/l	301.0 ± 81.1	241.0 ± 85.7	256 ± 91.8
dU-urate	3.95 (476)	3.01 (243)	3.22 (132)
mmol/d	3.78 ± 1.34	3.03 ± 1.25	3.02 ± 1.34
dU-Na	215.2 (475)	158.3 (262)	185.3 (136)
mmol/d	207.9 ± 80.3	147.2 ± 82.1	166.8 ± 94.0
dU-oxalate	0.370 (447)	0.365 (61)	0.356 (45)
mmol/d	0.360 ± 0.116	0.330 ± 0.153	0.360 ± 0.098
S-P	0.962 (467)	1.084 (243)	1.053 (131)
mmol/l	0.940 ± 0.204	1.040 ± 0.281	1.060 ± 0.173
dU-P	29.93 (467)	22.61 (243)	24.48 (131)
mmol/d	28.84 ± 10.52	21.50 ± 9.29	22.84 ± 10.73
P-threshold	0.889 (467)	1.029 (243)	0.986 (131)
mmol/l	0.880 ± 0.241	0.980 ± 0.309	0.980 ± 0.209

Group I: calcium oxalate kidney stone formers; group II: patients with verified osteoporosis; group III: patients examined for different reasons, without stones, without osteoporosis. Every cell of the table contains the median with the number of measurements in parentheses in the first row and the mean ± standard deviation in the second. dU-Ca, dU-urate, dU-Na, dU-oxalate and dU-P are daily outputs of calcium, urate, sodium, oxalate and phosphate, respectively; S-urate and S-P are serum concentrations of urate and phosphate; P-threshold is the renal phosphate threshold.

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Table 2. The effect of thiazides introduction and withdrawal

	δdU-Ca mmol/d	δU-Ca/U-cr mmol/mmol	δdU-Ca/mass mmol/kg
Introduction			
Mean	-1.819	-0.106	-21.500
SD	3.183	0.247	42.629
p	0.001	0.013	0.004
Withrawal			
Mean	0.975	0.083	12.200
SD	3.023	0.233	41.723
p	0.078	0.048	0.103

Thiazides were introduced in patients with a mean daily calcium output of 10.03 mmol/d (3.61) and withdrawn in patients with a mean output of calcium of 8.17 mmol/d (3.20). The absolute difference (δ) was calculated as the second measurement minus the first measurement, whereas the significance (p) was tested with the use of paired T-test. δdU-Ca is the absolute difference in the calcium output, δU-Ca/U-cr is the absolute difference in the ratio of calcium to creatinine in urine, δdU-Ca/mass is the absolute difference in the ratio of output of calcium to the mass of the patient in kg.

Results

The target population stabilized for ten years and patients with oxalate stones prevail. Table 1 describes the distribution of basic parameters of oxalate stone formers in comparison with two other groups of patients having no episode of kidney stones.

Group I consists of 508 determinations in calcium-oxalate kidney stone formers (whewellit, weddellit or a mixture of both), group II comprises 162 determinations in patients with osteoporosis (verified by densitometry or X-ray investigation) and group III consists of 297 determinations in patients evaluated for different reasons (the most frequent clinical question in this particular group was "is there anything with calcium or phosphate?", but without osteoporosis and without stones.

The effectiveness of thiazides on hypercalciuria was tested in a retrospective trial in which the effect of the introduction and the withdrawal of thiazides was studied. All patients treated with thiazides were included in this trial. However, the majority of them were kidney stone formers.

Results are summarized in table 2. Patients were tested with respect to the introduction of thiazides (i.e. paired values before and after thiazides, mean time interval 139±69 days, N = 37) and withdrawal (i.e. with and without thiazides, time interval 218 ±180 days, N = 33).

The effect of allopurinol on uric acid parameters was tested in the retrospective trial of the similar protocol, and 100 mg of allopurinol was introduced or withdrawn. The introduction of allopurinol (number of patients N = 41) resulted in a decrease of serum urate (S-urate, from 376 to 312 µmol/l), daily output of urate (dU-urate, from 4.02 to 3.33 mmol/d), the ratio of urine urate to urine creatinine (U-urate/U-cr, from 0.28 to 0.25 mmol/mmol) and the ratio of the daily urate to the patient mass (dU-urate/mass, from 51.0 to 42.3 mmol/kg). The withdrawal of allopurinol (N = 24) resulted in an increase in all the above-mentioned parameters: S-urate from 300 to 332 µmol/l, dU-urate from 3.29 to 3.60 mmol/d, U-urate/U-cr from 0.23 to 0.28 mmol/mmol and dU-urate/mass from 41.9 to 46.0 mmol/kg.

The effect of magnesium supplementation was tested in a similar manner, and only negligible changes in serum and a small increase in urine were seen.

Supplementation of phosphates (in the form of buffer) increased serum phosphate only slightly, but the output of phosphate increased significantly. Reverse changes were observed upon withdrawal of magnesium or phosphate supplementation.

Finally, we studied the differences in fluid intake among all groups of patients. The mean volume of urine was 2123 ml per day in group I, 1646 ml in group II and only 1497 ml in group III, respectively.

Discussion

As can be seen from table 1, there is a strong tendency among oxalate stone formers (Group I) towards

- hypercalciuria;
- hypernatriuria;
- hyperuricosuria;
- increased blood urate;
- hyperphosphaturia, with decreased renal phosphate threshold.

Surprisingly, there is a similar output of oxalate in all groups, with only a slight tendency towards hyperoxaluria in oxalate stone formers and in some patients with decreased output of calcium (group III).

Thiazides and allopurinol were prescribed only in carefully selected cases, and under strict control of possible side effects.

The mean decrease of calcium output after the introduction of hydrochlorothiazide (50 mg) was significant, but hypercalciuria normalized only in a minority of the patients (table 2). Patient compliance should be taken into account when speaking about a relatively low decrease in calcium output after thiazides. Erective impotency was sometimes reported by treated men, but postural hypotension was mentioned rather exceptionally. The withdrawal of thiazides again led to an increase in calciuria. It should be noted, however, that treatment with thiazides for more than two years is probably dubious.

Allopurinol was given mainly in hyperuricaemia. However, the output of uric acid decreased with allopurinol, too. All patients undergoing withdrawal of allopurinol were instructed to continue with a low-purine diet. This accounts for the negligible effect of allopurinol withdrawal and, vice versa, demonstrates an important effect of low-purine diet. Output of magnesium and phosphate was dependent on the dose given. Magnesium lactate is prescribed frequently, due to negligible gastrointestinal problems.

The fluid intake is probably the most important factor in the prevention of kidney stones of all kinds. In our group, the mean volume of urine of more than 2000 ml per day in the ambulatory investigation protocol, is satisfactory. The "Stone-Clinic Effect" may probably play a role in our oxalate stone formers.

The introduction of the measurement of intact para-

thyrine was very important, and several cases of primary hyperparathyreoidism were found effectively. At the same time, we started with the measurement of bone markers. It should be stressed that decreased bone density is relatively frequent in patients with hypercalciuria (predominantly of the renal type). We have found that some oxalate stone formers with hypercalciuria have increased osteocalcin, PICP, ICTP, alkaline phosphatase, PTH and decreased bone density.

Literature

1. Resnick MI, Pak CYC. Urolithiasis. A medical and surgical reference. WB Saunders, Philadelphia, 1990.

Summary

Kidney stone clinic: ten years of experience. Jabor A. Ned Tijdschr Klin Chem 1996; 21: 8-10.
Experiences are described at a kidney stone clinic which was established as part of the Department of Clinical Biochemistry ten years ago. During this period, the investigational protocol has changed from an in-patient to an out-patient scheme. The most important metabolic abnormalities among calcium oxalate kidney stone formers were hypercalciuria, hypernatriuria, hyperuricosuria, increased blood urate, decreased blood phosphate and hyperphosphaturia with decreased renal phosphate threshold. These abnormalities were found in the majority of patients. Oxalate output was, however, increased in less than 50 percent of the patients. The effectivity of thiazides, allopurinol, magnesium and phosphate supplementation was tested, and it was concluded that (a) the effect of thiazides was significant, but calciuria normalized only in a few cases, (b) the withdrawal of allopurinol led to a significant increase of urate parameters only in patients without a low-purine diet, (c) a sufficient dose of magnesium and phosphate is necessary to achieve a therapeutic effect.
Preliminary data indicate that some patients with hypercalciuria and kidney stones are at risk of decreased bone mass, and the role of bone markers monitoring is mentioned.
Key-words: kidney stones; hypercalciuria; hyperuricosurie; thiazides; allopurinol.